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EXAMINER	
HOWARD, ZACHARY C	

ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/783,519	STASHENKO ET AL.	
	Examiner	Art Unit	
	Zachary C. Howard	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5 and 30-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5 and 30-33* is/are rejected.

7)☒ Claim(s) *4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/20/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 5/15/2006 has been entered in full. Claims 1, 3-5 and 30-33 are amended. Claims 2 and 17-29 are canceled. Claims 6-16 were previously canceled by Applicants on 2/20/04.

Claims 1, 3-5 and 30-33 are pending.

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 5/15/06 is acknowledged. All of the pending claims (1, 3-5 and 30-33) are in Group I, and therefore all of the pending claims are under consideration in the instant application. In view of Applicants' cancellation of the claims drawn to the other Groups, the restriction requirement is presently withdrawn; however, it will be reinstated if Applicants introduce new claims that are drawn to the subject matter of the canceled claims.

Specification

The disclosure is objected to because of the following informalities:

(1) An updated priority statement of the instant application's parent provisional and nonprovisional applications should be included in the first sentence of the specification or application data sheet. It is noted that the priority statement in the first sentence of the specification was amended 2/20/2004. However, the priority statement should now be amended to indicate that Application 09/618304 issued as U.S. Patent No. 6,777,537.

Appropriate correction is required.

Claim Objections

Claim 4 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 3 is drawn to an isolated polynucleotide encoding a polypeptide which is an osteoclast 116-kDA proton pump subunit, comprising the nucleotide sequence of SEQ ID NO: 1 or its complementary nucleotide sequence. Claim 4 depends from claim 3 and limits the polypeptide to comprising SEQ ID NO: 2. However, if the polynucleotide of claim 3 comprises SEQ ID NO: 1 or its complement, it would inherently encode a polypeptide comprising SEQ ID NO: 2 (i.e., SEQ ID NO: 2 is the protein encoded by SEQ ID NO: 1). Therefore, claim 4 does not further limit claim 3.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 32 and 33 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 32 and 33 as written, do not sufficiently distinguish over cells that exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. The host cells of claims 32 and 33 respectively encompass any host cell comprising the polynucleotide of claim 3 or 5. Each of claims 3 and 5

encompass an isolated nucleic acid of SEQ ID NO: 1. While this nucleic acid is isolated, dependent claims 32 and 33 encompass a host cell comprising an identical nucleic acid. The instant specification teaches that SEQ ID NO: 1 is found in human osteoclasts. Therefore, claims 32 and 33 do not sufficiently distinguish over naturally occurring osteoclasts comprising SEQ ID NO: 1. See Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, for example by indicating that the claimed cell contains an expression vector as taught on page 12, line 19 of the specification. See MPEP 2105.

Claim Rejections - 35 USC § 112, 1st paragraph, enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5 and 31-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide comprising SEQ ID NO: 1 or its complement, and an isolated or cultured cell comprising said polynucleotide, does not reasonably provide enablement for (1) a nucleotide sequence comprising nucleotides sequences which hybridize under conditions of medium or high stringency to SEQ ID NO: 1 or its complementary sequence; or (2) a non-isolated host cell comprising the claimed polynucleotides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and

8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The specification teaches that the polynucleotide of SEQ ID NO: 1 encodes the polypeptide of SEQ ID NO: 2, which is an osteoclast-specific proton pump subunit of 116 kDa. The specification asserts that the "cell-specific expression of OC-116kDa makes it useful as a target for therapeutic intervention in diseases with increased resorption of bone or cartilage, such as osteoporosis or osteoarthritis" (pg 3, lines 17-20). The relevant art supports this utility; specifically, Farina et al (2002) teaches, "the 116 kDa subunit is expressed exclusively in osteoclasts and confers unique functional and pharmacological properties to the osteoclast V-ATPase" and "[i]t was demonstrated that inhibition of this pump can abolish bone resorption; therefore, osteoclast-selective inhibitors could provide novel and useful agents for the treatment of osteoporosis" (see Abstract of Farina et al, 2002. Current Pharmaceutical Design. 8: 2003-2048.) In view of these teachings, the specification enables one of skill in the art to use the claimed polynucleotide of SEQ ID NO: 1 in order to produce the polypeptide of SEQ ID NO: 2, which can be used to screen for inhibitors of the pump. Claims 1, 2, 3 and 30 are limited to isolated polynucleotides comprising SEQ ID NO: 1.

However, claim 5 is directed to a broad genus of polynucleotides that encode an "osteoclast proton pump subunit" and comprise a nucleotide sequence that hybridizes to SEQ ID NO: 1 or its complement under conditions of medium or high stringency. Nucleotide sequences that will hybridize to the complement of SEQ ID NO: 1 include small fragments of SEQ ID NO: 1 ranging from several contiguous polynucleotides to the entire sequence of SEQ ID NO: 1. Furthermore, the polynucleotides of claim 5 "comprise" said fragments; therefore the claim encompasses said fragments as found within any longer sequences, such as variants of SEQ ID NO: 1 comprising a fragment that will hybridize to the complement of SEQ ID NO; 1. The specification does not provide a limiting definition of the term "osteoclast proton pump subunit". Therefore, this phrase does not limit the encoded polypeptide to a polypeptide having any particular function identical to the parent polypeptide of SEQ ID NO: 2.

The breadth of the language of the claims for any polynucleotide molecule that hybridizes under medium or high stringency conditions and "encodes an osteoclast proton pump subunit" is not commensurate in scope with the enablement provided by the specification. The term "hybridize" or "hybridization" generically refers to a process in which a strand of nucleic acid joins or matches up with a complementary strand through the process of base pairing, wherein the process is basically used to locate or identify DNAs encoding specific proteins. It is well established in the art that 15-20 bases have been considered sufficient to achieve this process. However, in some instances the conditions under which the hybridization is performed have an effect on the outcome of the hybridization. With these points in mind, and giving the claims their broadest reasonable interpretation, the claims encompass an extremely large number of polynucleotide sequences for which there is not sufficient enablement. As written, the claims encompass polynucleotide sequences that (1) are from different species; (2) are the result of degeneracy; (3) encode for biologically active SEQ ID NO: 2; 3) do not encode biologically active SEQ ID NO: 2; (4) encode any of a number of fragments, derivatives, or analogs of SEQ ID NO: 2 including those with any number of changes (deletions, insertions, or substitutions) to the amino acid sequence of SEQ ID NO: 2

The single example of an "osteoclast proton pump subunit" (SEQ ID NO: 2) provided in the specification does not provide a representative number of different polynucleotide sequences for the entire scope of the claims that would enable all of the above discussed polynucleotide sequences with assurances that they possess or encode proteins having the desired activity (i.e., function as the 116 kDa osteoclast proton pump subunit of SEQ ID NO: 2). Since the first paragraph of the statute under 35 USC 112 requires that there must be an enabling disclosure to support the breadth of the claims, a review of the specification confirms that the scope of the various polynucleotide sequences that are discussed above have not been enabled. In the absence of sufficient guidance, it would require undue experimentation to enable all of the sequences that are encompassed by the claims. It would time consuming to prepare all of these polynucleotides and test them for hybridization and functionality, and it would be unpredictable which changes could be made and retain activity.

Applicants have not given any guidance as to which amino acid substitutions, deletions or insertions to make to achieve any desired property, or defined a difference in structure, or difference in function, between the protein corresponding to SEQ ID NO: 2 and variants of said protein. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. Particular regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions [see Wells (18 September 1990) "Additivity of Mutational Effects in Proteins." Biochemistry **29**(37): 8509-8517; Ngo *et al.* (2 March 1995) "The Protein Folding Problem and Tertiary Structure Prediction, Chapter 14: Computational Complexity Protein Structure Prediction, and the Levinthal Paradox" pp. 492-495]. However, Applicants have provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions.

Although the specification outlines art-recognized procedures for producing variants, this is not adequate guidance as to the nature of active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, it may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art

recognizes that function cannot be predicted from structure alone [Bork (2000) "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle." Genome Research **10**:398-400; Skolnick and Fetrow (2000) "From gene to protein structure and function: novel applications of computational approaches in the genomic era." Trends in Biotech. **18**(1): 34-39; Doerks *et al.* (June 1998) "Protein annotation: detective work for function prediction." Trends in Genetics **14**(6): 248-250; Smith and Zhang (November 1997) "The challenges of genome sequence annotation or 'The devil is in the details'." Nature Biotechnology **15**:1222-1223; Brenner (April 1999) "Errors in genome annotation." Trends in Genetics **15**(4): 132-133; Bork and Bairoch (October 1996) "Go hunting in sequence databases but watch out for the traps." Trends in Genetics **12**(10): 425-427].

Due to the large quantity of experimentation necessary to generate the large number of variants recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Further, with respect to claims 32 and 33, these claims are directed to a broad genus of cells comprising the claimed polynucleotide. The specification contemplates methods of "treating bone mass disorders such as osteoporosis and osteoarthritis" (pg 13, lines 14-16) using the polypeptide encoded by the claimed polynucleotide. Furthermore, the genus of claimed cells includes those containing an expression vector expressing the claimed protein. Therefore, the genus of claimed cells encompasses those used in gene therapy. However, the specification does not teach any methods or working examples that indicate the claimed nucleic acid is introduced and expressed in a cell for therapeutic purposes. The disclosure in the specification is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. For example, the specification does not teach what type of vector would introduce the

claimed nucleic acid into the cell or in what quantity and duration. Relevant literature teaches that since 1990, about 3500 patients have been treated via gene therapy and although some evidence of gene transfer has been seen, it has generally been inadequate for a meaningful clinical response (Phillips, A., J Pharm Pharmacology 53: 1169-1174, 2001; abstract). Additionally, the major challenge to gene therapy is to deliver DNA to the target tissues and to transport it to the cell nucleus to enable the required protein to be expressed (Phillips, A.; pg 1170, ¶ 1). Phillips also states that the problem with gene therapy is two-fold: 1) a system must designed to deliver DNA to a specific target and to prevent degradation within the body, and 2) an expression system must be built into the DNA construct to allow the target cell to express the protein at therapeutic levels for the desired length of time (pg 1170, ¶ 1). Therefore, undue experimentation would be required of the skilled artisan to introduce and express the claimed nucleic acid into the cell of an organism to treat disease. Additionally, gene therapy is unpredictable and complex wherein one skilled in the art may not necessarily be able to introduce and express the claimed nucleic acid in the cell of an organism or be able to produce the encoded protein in that cell. Due to the large quantity of experimentation necessary to introduce and express the claimed nucleic acid in a cell of an organism for therapy, the lack of direction/guidance presented in the specification regarding how to introduce the claimed nucleic acid in the cell of an organism to be able produce the encoded protein, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art that establishes the unpredictability of transferring genes into an organism's cells, and the breadth of the claims which fail to recite any cell type limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope. Please note that this rejection could be overcome by amending the claims to recite, for example, "An isolated cell..." because such an amendment would clarify that the claims are directed only to cells that are to be made and used in culture.

Claim Rejections - 35 USC § 112, 1st paragraph, written description

Claims 5, 31 and 33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicants are claiming and what Applicants have possession of.

Claim 5 is directed to a broad genus of polynucleotides that encode an "osteoclast proton pump subunit" and comprise a nucleotide sequence that hybridizes to SEQ ID NO: 1 or its complement under conditions of medium or high stringency. Nucleotide sequences that will hybridize to the complement of SEQ ID NO: 1 include small fragments of SEQ ID NO: 1 ranging from several contiguous polynucleotides to the entire sequence of SEQ ID NO: 1. Furthermore, the polynucleotides of claim 5 "comprise" said fragments; therefore the claim encompasses said fragments as found within any longer sequences, such as variants of SEQ ID NO: 1 comprising a fragment that will hybridize to the complement of SEQ ID NO; 1. The specification does not provide a limiting definition of the term "osteoclast proton pump subunit". Therefore, this phrase does not limit the encoded polypeptide to a polypeptide having any particular function identical to the parent polypeptide of SEQ ID NO: 2.

Therefore, the genus of polynucleotide encompassed by claim 5 is highly variant because a significant number of structural differences between genus members are permitted. Claims 31 and 33 depend from claim 5 and encompass a similar genus of polynucleotides or cells comprising said genus of polynucleotides.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a

combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features, or critical conserved regions, of the genus of polypeptides encoded by the claimed polynucleotides. There is not even identification of any particular portion of the structure that must be conserved. Structural features that could distinguish encoded polypeptides in the genus from others in the protein class are missing from the disclosure. The specification and claims do not provide any description of what changes should be made. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides and polypeptides encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicants were not in possession of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until

reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only polynucleotides comprising SEQ ID NO: 1, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see pg 1115).

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 31 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms "medium stringency" and "high stringency" in claim 5 are relative terms which render the claim indefinite. The terms "medium stringency" and "high stringency" are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The specification teaches, "Stringency conditions which are appropriately termed "medium stringency" or "high stringency" are known to those skilled in the art or can be found in standard texts such as *Current Protocols in Molecular Biology*..." (pg 12, lines 1-3). However, this exemplary

teaching in the specification does not provide the claim with any sort of limitation as to what specific conditions (including hybridization and wash lengths of time, temperature and solutions) are encompassed by the terms "medium stringency" or "high stringency". For purposes of prosecution, these claims will be interpreted to encompass any polynucleotide that will hybridize to SEQ ID NO: 1 or its complement.

The remaining claims are rejected for depending from an indefinite claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3-5 and 30-33 are rejected under 35 U.S.C. 102(a) as being anticipated by Li et al, 1996 (January 26th). Biochemical and Biophysical Research Communications. 218: 813-821 (cited as reference AR on the 2/20/04 IDS). The earliest filing date to which the instant application claims priority is February 22nd, 1996. The reference of Li, although sharing two inventors with the instant Application, is considered to be invented by others because it has an author that is not included in the instant application.

In Figure 2 (pg 816), Li teaches a polynucleotide sequence of 2640 nucleotides that is identical to instant SEQ ID NO: 1. Further, the sequence taught by Li encodes a

polypeptide of 822 amino acids that is identical to instant SEQ ID NO: 2. For these reasons, Li anticipates instant claims 1 and 3-5.

Claims 30 and 31 encompass a polynucleotide of claim 5 operably linked to a regulatory sequence. Li also teaches 57 bases of the 5' untranslated region and ~120 bases of the 3' untranslated region of the proton pump gene (Figure 2, pg 816). These regions meet the definition of "regulatory sequence". Therefore, the teachings of Li anticipate claims 30 and 31.

Li further teaches that the polynucleotide sequence shown in Figure 2 was isolated from osteoclastoma tumor cells. Therefore, the osteoclastoma tumor cells as taught by Li anticipate instant claims 32 and 33.

Claims 32 and 33 are rejected under 35 U.S.C. 102(a) as being anticipated by Li et al, 1995 (August). J Bone Miner Res. 10(8): 1197-1202. The earliest filing date to which the instant application claims priority is February 22nd, 1996. The reference of Li, although sharing two inventors with the instant Application, is considered to be invented by others because it has four authors that are not included in the instant application.

Claims 32 and 33 each encompass a cell comprising a polynucleotide of SEQ ID NO: 1. The instant specification teaches that a polynucleotide comprising SEQ ID NO: 1 can be isolated from cells found in osteoclastoma tumor (pg 15, lines 12-25 and pg 16, lines 1-21). Therefore, these tumor cells inherently comprise a polynucleotide comprising SEQ ID NO: 1.

Li teaches isolated cells from osteoclastoma tumor ("Disaggregated tumor cells were passaged weekly for 4 weeks..." (pg 1199). Therefore, Li clearly anticipates instant claims 32 and 33.

Claims 5, 31 and 33 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Peng et al, 1994. Journal of Biological Chemistry. 269(25): 17262-17266 (cited as reference AY on the 2/20/04 IDS).

Claim 5 is drawn to a genus of isolated polynucleotides that encode a osteoclast proton pump subunit and comprise a polynucleotide sequence that hybridizes to SEQ ID NO: 1 or its complement under medium or high stringency conditions. The specification does not provide a limiting definition of the phrase "osteoclast proton pump subunit"; therefore the term encompasses any polypeptide with similarity to SEQ ID NO: 1, which the specification teaches as an example of an osteoclast proton pump subunit. Furthermore, it is noted that any fragment of SEQ ID NO: 1 (including small fragments such as 10 contiguous nucleotides) will hybridize to the complement of SEQ ID NO: 1 under high stringency conditions.

Peng teaches the nucleic acid and corresponding encoded amino acid sequence for a bovine vacuolar-type proton pump (Figure 2; pg 17264). The instant specification teaches that instant SEQ ID NO: 1 has 59.% homology with the bovine sequence taught by Peng (pg 9, lines 1-2). In view of the lack of a limiting definition of the term "osteoclast proton pump subunit" in the instant specification, the encoded protein taught by Peng meets this claim limitation. Furthermore, the nucleic acid taught by Peng comprises sequences that would hybridize with the complement of instant SEQ ID NO: 1 under conditions of high stringency. For example, instant SEQ ID NO: 1 from residues 2197-2220 contains the 24 residue sequence "CAC CAG GCC ATC CAC ACC ATC GAG" and the nucleic acid sequence taught by Peng from residues 2281-2304 contains the identical sequence "CAC CAG GCC ATC CAC ACC ATC GAG." Therefore, the nucleic acid sequence taught by Peng comprises a sequence that would hybridize with the complement of SEQ ID NO: 1 under conditions of high stringency. For these reasons, the nucleic acid taught by Peng anticipates instant claim 5.

Claim 31 encompasses a polynucleotide of claim 5 operably linked to a regulatory sequence. Peng also teaches 120 bp of the 5' untranslated region and 501 bp of the 3' untranslated region of the proton pump gene (Figure 1, pg 17264). These regions meet the definition of "regulatory sequence". Therefore, the teachings of Peng anticipate claim 31.

Claim 33 encompasses a cell comprising a polynucleotide of claim 5. Peng teaches that the nucleic acid sequence shown in Figure 2 was isolated from bovine

brain. Therefore, bovine brain cells inherently comprise the nucleic acid sequence shown in Figure 2, and the teachings of Peng anticipate claim 33.

Claim 5, 31 and 33 are rejected under 35 U.S.C. 102(e) as being anticipated by Stashenko et al, U.S. Patent No. 5,552,281, published 9/3/1996, filed 2/23/1995, and claiming priority as a continuation to a filing date of 4/6/1993.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Stashenko teaches SEQ ID NO: 25, which is a polynucleotide of 151 nucleic acid residues. SEQ ID NO: 25 of Stashenko is 100% identical to the complement to residues 2472-2632 of instant SEQ ID NO: 1. Therefore, SEQ ID NO: 25 of Stashenko would hybridize to instant SEQ ID NO: 1 under conditions of high stringency. The specification does not provide a limiting definition of the phrase "osteoclast proton pump subunit"; therefore the term has been interpreted to encompasses any polypeptide with similarity to SEQ ID NO: 1, including fragments of said polypeptide such as that encoded by SEQ ID NO: 25 of Stashenko. Therefore, SEQ ID NO: 25 of Stashenko clearly anticipates instant claim 5.

Stashenko further teaches DNA constructs directing expression of isolated DNA sequences encoding DNA sequences of the invention including SEQ ID NO: 25 (column 1, lines 39-46), and host cells comprising said DNA constructs (column 1, lines 47-57). Said constructs and host cells clearly anticipate instant claims 31 and 33.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 5, 31 and 33 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2 and 4 of U.S. Patent No. 6,403,304. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Claim 2 of the '304 patent encompasses a DNA construct comprising SEQ ID NO: 25, which is a polynucleotide of 151 nucleic acid residues. SEQ ID NO: 25 of the '304 patent is 100% identical to the complement to residues 2472-2632 of instant SEQ ID NO: 1. Therefore, SEQ ID NO: 25 of '304 patent would hybridize to instant SEQ ID NO: 1 under conditions of high stringency. The specification does not provide a limiting definition of the phrase "osteoclast proton pump subunit"; therefore the term has been interpreted to encompasses any polypeptide with similarity to SEQ ID NO: 1, including fragments of said polypeptide such as that encoded by SEQ ID NO: 25 of the '304 patent. Furthermore, claim 2 requires that the DNA sequence includes regulatory sequences operably linked to SEQ ID NO: 25. Therefore, claim 2 of the '304 patent anticipates both instant claim 5 and 31.

Claim 5 of the '304 patent is drawn to a cell comprising a DNA construct comprising SEQ ID NO: 25 linked to a regulatory sequence. Therefore, claim 5 anticipates instant claim 33.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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